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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/754,997	01/04/2001	J. Michael Salbaum	P-NI 4552	4685

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/754,997	SALBAUM, J. MICHAEL	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *1-8 and 16-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-15 and 20-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. ~~37 CFR 1.78.~~

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9/11/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendment, filed 9/11/03, is acknowledged.

2. Claims 1-42 are pending.

3. Claims 1-8 and 16-19 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Since the cited prior art is no longer anticipates or renders obvious the elected species of the amended claims, the Examiner extended the search to include all the species.

4. Claims 9-10, 11-15 and 20-42 are under examination as they read on an isolated nucleic acid molecule of SEQ ID NO: 1 encoding Nope polypeptide of SEQ ID NO: 2 and SEQ ID NOs: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23 and oligonucleotides 300-325, 325-350 and 300-350 as the species.

5. 35 U.S.C. § 101 reads as follows:

> *"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".*

6. Claims 9-10, 11-15 and 20-42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility.

The final utility guidelines published Jan. 2001 and corresponding training materials (available on the PTO Website), none of the disclosed uses is a specific and/or substantial use.

The instant application has provided a description of an isolated polynucleotide. The instant application does not disclose the biological role of the polynucleotide or its significance. The instant specification asserts specific utilities for the claimed invention, for the development of the nervous system and related biological functions (on pages 3, lines 3-6), as tumor suppressor (page 37, lines 3), to identify individuals at increased risk of developing a proliferative disease, such as cancer (page 37, lines 9-10 in particular) and diagnoses of Bardel-Biedl syndrome (page 38, lines 20-21). The specification also asserts that the claimed immunoglobulin superfamily member protein is acknowledged by the Applicants to be related to having diverse intracellular signaling domain (see page 51, line 16) and proteins containing Ig are disclosed to be involved with neuronal cell adhesion molecules (see page 50, line 12).

These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for Nope polynucleotide. The disclosed polypeptide encoded by the claimed polynucleotide is said to have a potential function

based upon its amino acid sequence similarity to other known proteins. After further research, specific and substantial utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner V. Manson*, 148 U.S. P. Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this board interpretation was not the intended definition of "useful" as it appears in 35 U.S. C. § 101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility.

The nucleic acid of the instant invention and the protein encoded thereby are compounds which share some structural similarity with Punc (45% sequence identity in the region ranging from the beginning of the second ig domain through the first FnIII repeat), DCC, Neogenin, and UNC-40 proteins based on sequence similarity. It is not clear if the protein encoded by the claimed nucleic acid of the instant application would have the same function in axonal guidance. Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentablility. Since the instant specification does not disclose a credible "real world" use for Nope, then the claimed invention as disclosed does not meet the requirement of 35 U.S.C. § 101 as being useful.

The instant claims are drawn to a nucleic acid encoding a polypeptide of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the Nope polynucleotide of the instant application was, as of the filling date, useful to identify an individual predisposed to developing cancer and increased risk of developing a proliferative disease, or diagnoses of Bardel-Biedl syndrome. Until some actual and specific significance can be attributed to the nucleic acid encoding the protein identified in the specification as Nope, one of ordinary skill in the art would be required to perform additional

experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

No single effect of the disclosed Nope polynucleotide is ascribed to the claimed protein. Note that while the specification produces the full-length protein recombinantly, no biological activity is established for the full length protein or any of the claimed fragments thereof. As such, further research would be required to identify or research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved would be required. Since the instant specification does not disclose a "real world" use for Nope, then the claimed invention as disclosed does not meet the requirements of 35 U.S. C. § 101 as being useful.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 9-10, 11-15 and 20-42 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Further, the specification does not provide sufficient enablement for how to make any nucleic acid molecule encoding a Nope polypeptide of SEQ ID NO: 2 or "modification" of the encoding nucleic acid sequence or a modification of SEQ ID NO:1 in claims 9-10; the isolated nucleic acid molecule "comprising" nucleotide sequence SEQ ID NOs: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 in claims 11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action mailed 03/10/2003.

Applicant's arguments, filed 09/11/2003, have been fully considered, but have not been found convincing.

Applicant asserts that the specification teaches that a modification of a nucleic acid can include one or several nucleotide addition, deletions, or substitutions with respect to a reference sequence, including a substantially the same nucleotide sequence that can hybridize under moderately stringent or higher stringency conditions. Applicant concludes that the specification provides sufficient description and guidance to enable the claimed nucleic acid molecules and

modifications thereof. Applicant contests the rejection with respect to the assertion that one skilled in the art would not be able to determine which nucleic acid sequences encompassed by the claims would be useful for detection of SEQ ID NO:1.

However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the nucleic acid which are tolerant to change (e.g. such as by nucleic acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Due to the large quantity of experimentation necessary to obtain such "modification" of Nope polynucleotide variants, to generate the infinite number of derivatives recited in the claims and to determine the specific activity of the infinite variants, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the state of the prior art which establishes that biological activity cannot be predicted based on structural similarity, and the breadth of the claims which embrace a broad class of structural variants, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

9. Claims 9-10 and 14 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed 03/10/2003.

Applicant's arguments, filed 09/11/2003, have been fully considered, but have not been found convincing

Applicant asserts that the specification teaches that a modification of a nucleic acid can include one or several nucleotide addition, deletions, or substitutions with respect to a reference sequence, including a substantially the same nucleotide sequence that can hybridize under moderately stringent or higher stringency conditions. Applicant concludes that the specification provides sufficient written description and guidance to enable the claimed nucleic acid molecules and modifications thereof and for oligonucleotide consisting of at least 300 contiguous nucleotides of SEQ ID NO:1.

However, Applicant fails to satisfy the written-description requirement where the claimed invention called for a "modification" and "nucleic acid molecule comprising SEQ ID NOs:3, 5,...", but did not disclose such "variants" and any nucleic acid "comprising" such "SEQ ID NOs: 3, 5, 7...". The court stated that "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, what is required is a description of the DNA itself." *Fiers* 984 F.2d at 1170.

10. The declaration by Dr. Salbaum under 37 CFR 1.131 filed 9/11/03, (the declaration should have been filed under 1.132, see *In re Katz*, 687.450, 215 USPQ 14 (CCPA 1982)) is sufficient to overcome the rejection of claims 9, 10 and 12 based upon 35 U.S.C. 102(a) as set forth in the last Office action mailed 03/10/2003.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
December 11, 2003

Christina Chan

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